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EXAMINER	
SMITH, CAROLYN L	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 07/28/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/775,176	MCININCH, JAMES D.	
	Examiner	Art Unit	
	Carolyn L. Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-60* is/are rejected.

7)☒ Claim(s) *47, 55* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application is a continuation of abandoned application 09/698213. Cancelled claims 1-44 and new claims 45-60, filed 2/11/04, are acknowledged.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The present title is directed to computational nucleic acid coding and feature analysis, whereas in contrast the new claims are specifically directed to a method for determining the probability for one or more states for a selected nucleotide in a nucleic acid sequence.

Claims herein under examination are 45-60.

Claim Objections

Claims 47 and 55 are objected to because of the following informality: These claims fail to end in a period. Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 45-60 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Under the Interim Guidelines for Examination of Patent Applications for Patent Subject Matter Eligibility (published in the O.G. notice (1300 OG 142) on 11/22/2005) a method that does not result in a physical transformation of matter MAY be statutory where it recites a concrete, tangible and useful result; i.e. a practical application.

The instant claims are directed to a method for determining a probability for one or more states for a selected nucleotide in a nucleic acid sequence. It is noted that the method does not result in a physical transformation of matter, nor is any concrete, tangible and useful result produced/recited. Therefore, these claims are not statutory.

Claims Rejected Under 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

LACK OF WRITTEN DESCRIPTION

Claims 45-60 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time of the invention was filed, had possession of the claimed invention.

Applicant states that written support for the claims can be found in the specification on pages 17 (lines 17-20), 18 (lines 11-15), 21 (line 1) through 26 (line 26), 46 (line 1) through 48 (line 10), and Example 2.

Claims 45-48, 50-55, 57, and 60 recite the term "selected" which is not supported in the passages of the specification listed above. The specification states a single nucleotide, such as on page 21, line 8, but it makes no mention of whether this nucleotide was selected or randomly chosen.

Claims 45 (lines 12-13), 51 (lines 13-14), and 52 (lines 11-12) recite the phrase "wherein said bias function does not have the same value in all of said states for said selected nucleotide" which is not supported in the passages of the specification listed above. The scope of the claims is broader than the support found in the specification. For example, as stated on page 21, lines 1-6, bias can be the value of one for at least one state and a value other than one for at least one state. However, this does not provide written support that the bias function does not have the same value in all of said states, which can be reasonably interpreted to mean all values must be different.

Claims 50 and 60 recite the phrase bias "'function has a value' between 0.0 and 0.9, or greater than 1.1". It is unclear what the term "value" is intended to mean. If value is intended to mean "bias" then there is proper written support for this phrase on pages 18 (line 17) and 21 (line 6). However, if the term "value" is intended to mean the resultant value of the bias function, then there is no adequate written support for this term. Because proper claim examination involves using the broadest reasonable interpretation of the claims, the latter definition of "value" is encompassed in claims 50 and 60 which therefore makes the phrase "function has a value" a NEW MATTER issue.

Because the introduction of phrases "selected", "wherein said bias function does not have the same value in all of said states for said selected nucleotide", and "function has a value" lacks

written basis for amended claims 45-48, 50-55, 57, and 60, as filed on 2/11/04, these phrases are considered NEW MATTER. Claims 49, 56, and 58-59 are also rejected due to their dependency from claims 45 and 52.

Claim Rejections – 35 U.S.C. 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of the skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

LACK OF SCOPE OF ENABLEMENT

Claims 45-60 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the

art to which it pertains, or with which it is most nearly connected, to make and/or use the claimed invention.

Claims 45-60 are rejected because the specification, while being enabling for the following:

Initial oligonucleotide probability	p. 21, equation I,
Transition probability	p. 22, equation II,
Nucleic acid sequence probability	p. 23, equation III, and
Probability for each nucleotide state	p. 24, equation IV,

the specification does not reasonably provide enablement for any method of computation for determining the above probabilities. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The instant application fails to provide guidance to one of ordinary skill in the art for generating the probability values of the following by any other means than by the four equations indicated above. The specification does not provide or suggest what any other substitutable methods of computation could be for the above probability determinations thus not enabling one of ordinary skill in the art to know what calculations to perform. While the specification provides some guidance for a method of determining a probability value for the above listing using the particular equations or values disclosed, the specification does not provide guidance for a method of determining the probability by any other means. The specification does not provide working examples of the methods described using any other means of computing the described probability values. While working examples are not, per se, required, the specification must

provide adequate guidance such that one of skill in the art could practice the invention without undue experimentation. Given the lack of descriptive working examples in the specification, and the unpredictability of generating probability values, the specification as filed is not enabling for any method of determining the listed probability values as claimed. The instant application is only enabled for the above-mentioned computational means of the four probabilities.

Claims Rejected Under 35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 47-48, 50-51, 55, 57, and 60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claims 47 and 55, as currently written, each contain a mathematical equation that is confusing, because the equation incorporates "Φ (f)" representing bias function that effectively cancels itself out in the equation, and therefore nullifies its effect on the equation.

Claims 47 and 55 are vague and indefinite due to the lack of clarity in the following terms: f, S, P_f, P_i, and Φ. It is unclear as to what are the metes and bounds of these terms. A listing of the exact definitions of these terms in claims 47 and 55 would clarify this issue.

Claim 48 recites the term "middle nucleotide in said nucleic acid sequence" which is vague and indefinite. It is unclear what would be considered a middle nucleotide if said nucleic

acid is made up of *n* number of nucleotides where *n* is an even integer. Clarification of a "middle nucleotide" in this situation is requested.

Claims 50 and 60 (lines 1-2 of each) recite the phrase "bias function has a value between 0.0 and 0.9, or greater than 1.1" which is vague and indefinite. It is unclear if the "value" is intended to mean the resultant value of the bias function or if it is intended to mean the bias which is a value used in the bias function (as stated on page 18, line 17, of the specification). Clarification of the phrase, particular the intended meaning of "value" is requested via clearer claim wording.

Claim 51, line 12, recites the phrase "accepts a bias function" which is vague and indefinite. It is unclear if the determination step, the probability, or each state is accepting the bias function. Clarification of the metes and bounds of this phrase via clearer claim wording is requested.

Claim 57, line 2, recites the phrase "middle nucleotide in its own window" which is vague and indefinite. It is unclear what would be considered a middle nucleotide if said window contains *n* number of nucleotides where *n* is an even integer. Clarification of a "middle nucleotide" in this situation is requested.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention

was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 45-46, 48-54, and 56-60 are rejected under 35 U.S.C. 103(a) as being obvious over Borodovsky et al. (Computers Chemistry, Volume 17, No. 2, pages 123-133) in view of Selifonov et al. (US 2002/0183934 A1).

Borodovsky et al. describe a computer-implemented method (GENMARK) for determining different state probabilities of a nucleotide in a nucleic acid sequence using non-homogeneous Markov models, including initial and transitional probabilities (abstract and page 128, col. 1) as stated in claims 45 and 51-52. Borodovsky et al. analyze a nucleotide fragment "F" (page 129, col. 2, paragraph 3) of the nucleic acid sequence of interest, as stated in claims 49 and 56. Borodovsky et al describe using Markov chain models of coding and non-coding regions with a moving window of 96 basepairs with consequent steps moving 6 basepairs (page 125, col. 2, 3rd full paragraph). Borodovsky et al. describe probability values calculated for every nucleotide fragment F found in the window opening (window probabilities as well as nucleic acid sequence probabilities) which represents repeating steps a) through d) of claim 52 for remaining nucleotides. Borodovsky et al. refer to the fragment's middle point (page 129, col. 2, paragraph 1), as stated in claims 48 and 57. Borodovsky et al. describe varying window sizes of 48 to 94 nucleotides in length (page 129, col. 1, last line) which represents a window "of about 75 to 125 nucleotides" in length, as stated in claim 59. The GENMARK method is a program (page 132, col. 2, 2nd full paragraph) which represents a program storage device readable by machine. Borodovsky et al. describe generating a model DNA sequence moving left to right or right to left to define the probability of a nucleotide string (page 128, col. 1, paragraphs 2-3)

which represents a determination of nucleic acid sequence probabilities as well as performing step e) of claim 52 sequentially on contiguous nucleotides, as stated in claim 53. Borodovsky et al. describe using an inhomogenous Markov model having eight states including first, second third positive and negative strands as well as non-coding positive and negative strands (Figure 2 and its caption and page 125, col. 2, fourth paragraph), as stated in instant claims 46 and 54. However, Borodovsky et al. do not specifically state the application of a bias function to nucleic acid sequence probabilities wherein the bias function does not have the same value in all states for a selected nucleotide or the extending step of instant claim 58.

Selifonov et al. describe methods of generating a diverse population of character strings relating to a biological polymer wherein in these strings are generated by altering pre-existing character strings (page 2, paragraph 0014). Selifonov et al. describe the synthesized character strings are selected for one or more activity and a bias may be applied by filtering to display polymers above a desired threshold (page 2, paragraph 0015). Selifonov et al. describe biasing a selected group of strings (page 6, paragraph 0075). Selifonov et al. describe using a bias that imposes discriminating criteria for use of any genetic operators, and various types of positive and negative biases, such as sequence specific features (page 6, paragraph 0080). Selifonov et al. describe biasing character strings with members above a desired threshold (claim 83) and thresholds and a cutoff of 100 (paragraph 0083) which represents a bias function greater than 1.1, as stated in instant claims 50 and 60. Selifonov et al. describe replicating, reproducing and producing additional copies of parental population strings (paragraph 0075) and expanding nucleic acid sequence if window extends beyond either end via copying until the end of the sequence (paragraph 0225), which represents the extending step of instant claim 58.

Borodovsky et al. state the problem of predicting gene locations in newly sequenced DNA is well known but not resolved (abstract). Borodovsky et al. state large-scale DNA sequencing calls for fast and efficient gene recognition methods to find new genes (page 123, col. 1, lines 1-4). Borodovsky et al. state further improvements of the Markov chain/Bayes method for searching for genes (page 123, col. 2, lines 3-6). Selifonov et al. state rapid evolution of nucleic acids provides for the generation of encoded molecules with new and/or improved properties of industrial, agricultural, and therapeutic importance (page 1, paragraph 0008). Selifonov et al. provide new "in silico" methods modeled in a computer system for guided gene synthesis to avoid physical manipulation of nucleic acids including alterations in pre-existing character strings (page 2, paragraphs 0013 and 0015). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to make further improvements in gene searching programs, as stated by Borodovsky et al., by adding filtering techniques to in order to make searches more efficient. Therefore, a person of ordinary skill in the art would have been motivated to apply a bias to character strings (nucleic acids), as stated by Selifonov et al., to a gene predicting program, as stated by Borodovsky et al., in order to make methods faster and more efficient for discovering new genes (Borodovsky et al., page 123, col. 1, paragraph 1).

Thus, Borodovsky et al., in view of Selifonov et al., make obvious claims 45-46, 48-54, and 56-60.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (571) 272-0811.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tiffany Tabb whose telephone number is (571) 272-0556.

July 18, 2006

Carolyn Smith
Examiner
AU 1631